EXHIBIT A

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BlueCross BlueShield of Tennessee Medical Policy Manual

Proton Beam Therapy

DESCRIPTION

Proton beam therapy is a type of particulate radiation therapy that differs from conventional electromagnetic and/or photon radiation therapy. The use of protons is produced by an accelerator (cyclotron, synchrotron, synchrocyclotron, or linear). This type of radiation is proposed to allow for minimal scattering as particulate beams pass through tissue disposing ionizing energy at precise depths (i.e., the Bragg peak) to minimize tissue damage in the surrounding area.

Please note: For this specific policy, pediatric age is defined as age 21 and younger.

POLICY

- Proton beam therapy is considered medically necessary if the medical appropriateness criteria are met. (See Medical Appropriateness below.)
- Proton beam therapy for the treatment of all other conditions/diseases, including, but not limited to, the following is considered *investigational* unless there are unique clinical circumstances applicable to a specific member that would make use of proton beam therapy medically appropriate:
 - Anal canal cancer
 - Bladder cancer
 - Breast cancer
 - · Cervical and endometrial cancer
 - CNS cancer, primary (other than pediatric malignancies)
 - Esophageal cancer
 - Gastric Cancer
 - Head and neck cancer (other than those listed as medically appropriate)
 - Hodgkin's Lymphoma
 - Malignancies requiring craniospinal irradiation (other than pediatric malignancies)
 - Non-Hodgkin's Lymphoma
 - Non-small cell lung cancer (NSCLC) at any stage or for recurrence
 - Pancreatic cancer
 - Prostate cancer
 - Rectal cancer
 - · Retroperitoneal sarcoma
 - Sarcoma
 - Seminoma
 - Thymomas and thymic carcinoma

MEDICAL APPROPRIATENESS

- Proton beam therapy is considered medically appropriate if ANY ONE of the following criteria are met:
 - Primary therapy for uveal melanoma when considered preferential to brachytherapy
 - Postoperatively for the treatment of localized chordoma or chondrosarcoma of the base of the skull or cervical spine
 - Maxillary sinus or paranasal/ethmoid sinus cancer/tumors
 - Localized unresectable hepatocellular carcinoma or intrahepatic cholangiocarcinoma when sparing normal tissue cannot be adequately achieved with photon-based radiotherapy.
 - Treatment of pediatric malignancies

IMPORTANT REMINDERS

- Any specific products referenced in this policy are just examples and are intended for illustrative purposes only. It is not intended to be a recommendation of one product over another and is not intended to represent a complete listing of all products available. These examples are contained in the parenthetical e.g. statement.
- We develop Medical Policies to provide guidance to Members and Providers. This Medical Policy relates only to the services or supplies described in it. The existence of a Medical Policy is not an authorization, certification, explanation of benefits or a contract for the service (or supply) that is referenced in the Medical Policy. For a determination of the benefits that a Member is entitled to receive under his or her health plan, the Member's health plan must be reviewed. If there is a conflict between the Medical Policy and a health plan or government program (e.g., TennCare), the express terms of the health plan or government program will govern.

ADDITIONAL INFORMATION

For the treatment of localized prostate cancer, as well as other listed conditions considered investigational, proton beam therapy has not been shown to be superior to conventional radiation therapy at this time. Further randomized controlled studies are needed.

SOURCES

A phase III randomized trial of proton versus photons for hepatocellular carcinoma. *NRG Oncology: NRG-GI003*. Last update posted March 28, 2023. Retrieved April 4, 2023 from https://www.nrgoncology.org/Clinical-Trials/Protocol/nrg-gi003?filter=nrg-gi003.

American Society for Radiation Oncology. (2023). ASTRO model policies. *Proton beam therapy (PBT)*. Retrieved May 2, 2023 from https://www.astro.org/uploadedFiles/ MAIN SITE/Daily Practice/Reimbursement/Model Policies/Content Pieces/ASTROPBTModelPolicy.pdf.

Chao, H., Berman, A., Simone, C., Ciunci, C., Gabriel, P., Lin, H., et al. (2017). Multi-institutional prospective study of reirradiation with proton beam radiotherapy for locoregionally non-small cell lung cancer. *Journal of Thoracic Oncology: official publication of the international association for the study of lung cancer,* 12 (2), 281-292. (Level 2 evidence)

Chi, A., Chen, H., Wen, S., Yan, H., & Liao, Z. (2017). Comparison of particle beam therapy and stereotactic body radiotherapy for early stage non-small cell lung cancer: a systematic review and hypothesis-generating meta-analysis. *Radiotherapy and Oncology,* 123 (3), 346-354. (Level 1 evidence)

Falkson, C., Vella, E., Yu, E., El-Mallah, M., Mackenzie, R., Ellis, P., & Ung, Y. (2017). Radiotherapy with curative intent in patients with early-stage, medically inoperable, non-small-cell lung cancer: a systematic review. *Clinical Lung Cancer*, 18 (2), 105-121. (Level 1 evidence)

Habl, G., Uhl, M., Katayama, S., Kessel, K., Hatiboglu, G., Hadaschik, B., et al. (2016). Acute toxicity and quality of life in patients with prostate cancer treated with protons or carbon ions in a prospective randomized phase II study – the IPI trial. *International Journal of Radiation Oncology, Biology, Physics*, 95 (1), 435-443. Abstract retrieved November 30, 2016 from PubMed database.

Igaki, H., Mizumoto, M., Okumura, T., Hasegawa, K., Kokudo, N., & Sakurai, H. (2017). A systematic review of publications on charged particle therapy for hepatocellular carcinoma. *International Journal of Clinical Oncology,* 23 (3), 423-433. Abstract retrieved September 28, 2017 from PubMed database.

Kalogeridi, M., Zygogianni, A., Kyrgias, G., Kouvaris, J., Chatziioannou, S., Kelekis, N., & Kouloulias, V. (2015). Role of radiotherapy in the management of hepatocellular carcinoma: a systematic review. *World Journal of Hepatology*, 7 (1), 101-112. (Level 1 evidence)

Leroy, R., Benahmed, N., Hulstaert, F., Van Damme, N., & De Ruysscher, D. (2016). Proton therapy in children: a systematic review of clinical effectiveness in 15 pediatric cancers. *International Journal of Radiation Oncology and Biological Physics*, 95 (1), 267-278. Abstract retrieved November 30, 2016 from PubMed database.

Matloob, S., Nasir, H., & Choi, D. (2016). Proton beam therapy in the management of skull base chordomas: systematic review of indications, outcomes, and implications for neurosurgeons. *British Journal of Neurosurgery,* 30 (4), 382-387. Abstract retrieved November 30, 2016 from PubMed database.

National Comprehensive Cancer Network. (2022, April). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 2.2022. *Melanoma: Uveal.* Retrieved March 20, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2022, December). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Head and neck cancers*. Retrieved March 14, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2022, December). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Thymomas and thymic carcinomas*. Retrieved March 20, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2022, September). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 2.2023. *Bone cancer*. Retrieved March 14, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2022, September). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 2.2022. *Central nervous system cancers*. Retrieved March 14, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2022, September). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Prostate cancer.* Retrieved March 16, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2023, February). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 2.2023. *Non-small cell lung cancer*. Retrieved March 15, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2023, January). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Testicular cancer*. Retrieved March 16, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2023, March). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Biliary tract cancers*. Retrieved March 15, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2023, March). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 2.2023. Esophageal and esophagogastric junction cancers. Retrieved March 14, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2023, March). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Hepatocellular carcinoma*. Retrieved March 15, 2023 from the National Comprehensive Cancer Network.

National Comprehensive Cancer Network. (2023, March). NCCN Clinical Practice Guidelines in Oncology (NCCN Guideline®). Version 1.2023. *Soft tissue sarcoma*. Retrieved March 16, 2023 from the National Comprehensive Cancer Network.

Patel, S., Wang, Z., Wong, W., Murad, M., Buckey, C., Mohammed, K., et al. (2014). Charged particle therapy versus photon therapy for paranasal sinus and nasal cavity malignant diseases: a systematic review and meta-analysis. *Lancet Oncology,* 15 (9), 1027-1038. Abstract retrieved March 27, 2017 from PubMed database.

Pennicooke, B., Laufer, I., Sahgal, A., Varga, P., Gokaslan, Z., Bilsky, M., & Yamada, Y. (2016). Safety and local control of radiation therapy for chordoma of the spine and sacrum: systematic review. *Spine*, 2016 Aug 8 [Epub ahead of print]. Abstract retrieved September 28, 2016 from PubMed database.

Qi, W., Fu, S., Zhang, Q., & Guo, X. (2015). Charged particle therapy versus photon therapy for patients with hepatocellular carcinoma: a systematic review and meta-analysis. *Radiotherapy and Oncology: Journal of the European Society for Therapeutic Radiology and Oncology,* 114 (3), 289-295. (Level 1 evidence)

Verma, V., Lin, S., Simone, C., & Mehta, M. (2016). Clinical outcomes and toxicities of proton radiotherapy for gastrointestinal neoplasms: a systematic review. *Journal of Gastrointestinal Oncology*, 7 (4), 644-664. (Level 2 evidence)

Verma, V., Rwigema, J., Malyapa, R., Regine, W., & Simone, C. (2017), Systematic assessment of clinical outcomes and toxicities of proton radiotherapy for reirradiation. *Radiotherapy and Oncology,* 2017 Sep 20. Doi: 10.1016/j.radonc.2017.08.005. [Epub ahead of print]. Abstract retrieved September 28, 2017 from PubMed database.

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Policies included in the Medical Policy Manual are not intended to certify coverage availability. They are medical determinations about a particular technology, service, drug, etc. While a policy or technology may be medically necessary, it could be excluded in a member's benefit plan. Please check with the appropriate claims department to determine if the service in question is a covered service under a particular benefit plan. Use of the Medical Policy Manual is not intended to replace independent medical judgment for treatment of individuals. The content on this Web site is not intended to be a substitute for professional medical advice in any way. Always seek the advice of your physician or other qualified health care provider if you have questions regarding a medical condition or treatment.

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